Insertions and deletions in the great tit genome

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01/05/18

Introduction

Insertions and deletions

- short INDELs: sections of DNA $<$ 50bp that are deleted or inserted in a genome
- deletion bias in most organisms
- deletions more deleterious than insertions

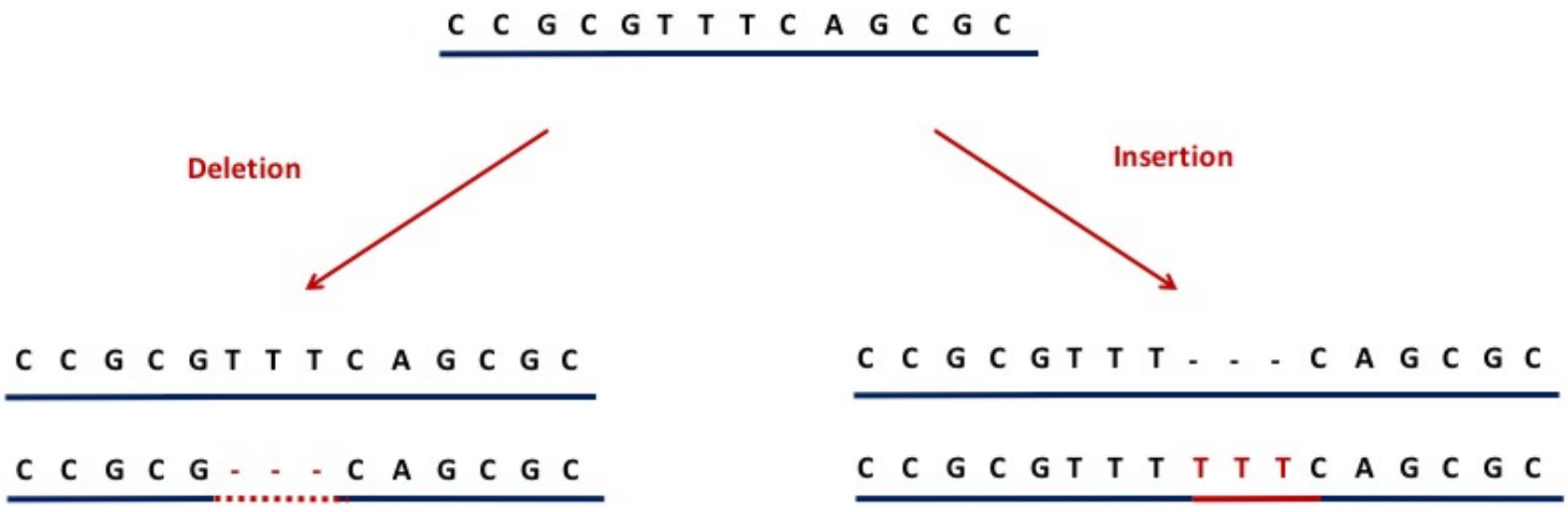

Figure 1: indel_diag

INDELs often overlooked

- Disproportionately occur in repetitive sequence
- Hard to align
- Often occur in hotspots
- 1/8 as frequent as SNPs in humans

(Earl et al., 2014; Montgomery et al., 2013)

The importance of INDELs in genome evolution

- Influence genome size:
  - low deletion rate $\rightarrow$ large genomes?
  - high deletion rate $\rightarrow$ compact genomes?

(Leushkin and Bazykin, 2013; Nam and Ellegren, 2012; Ometto et al., 2005; Sun et al., 2012)

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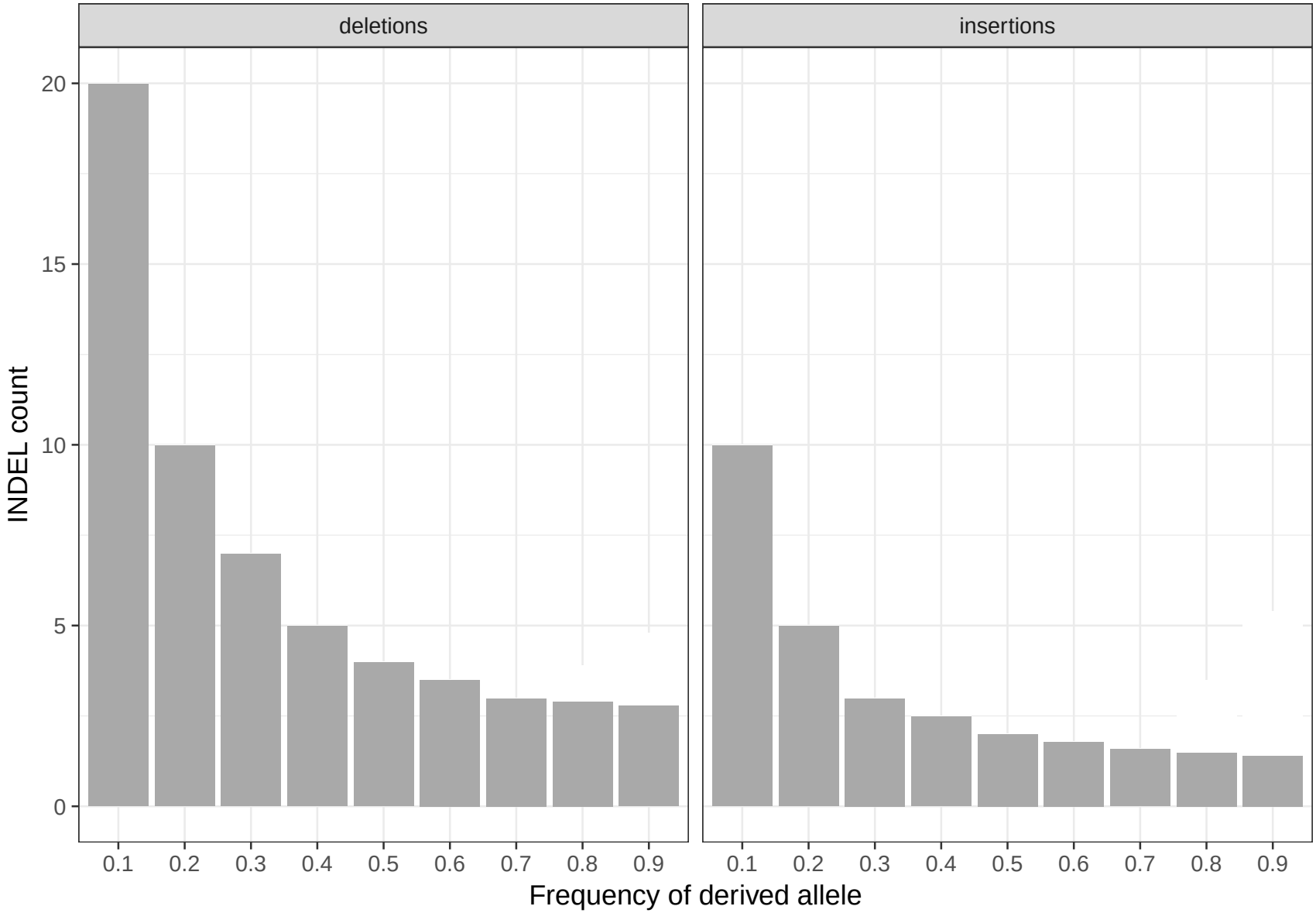
(Leushkin and Bazykin, 2013; Nam and Ellegren, 2012; Ometto et al., 2005; Sun et al., 2012)

INDEL mutation

INDEL selection

- Deletions
  -
- Insertions may be favoured:
  - biased gene conversion
  - minimum intron size
  - polarisation error

Importance of polarisation error



(see Hernandez et al., 2007)

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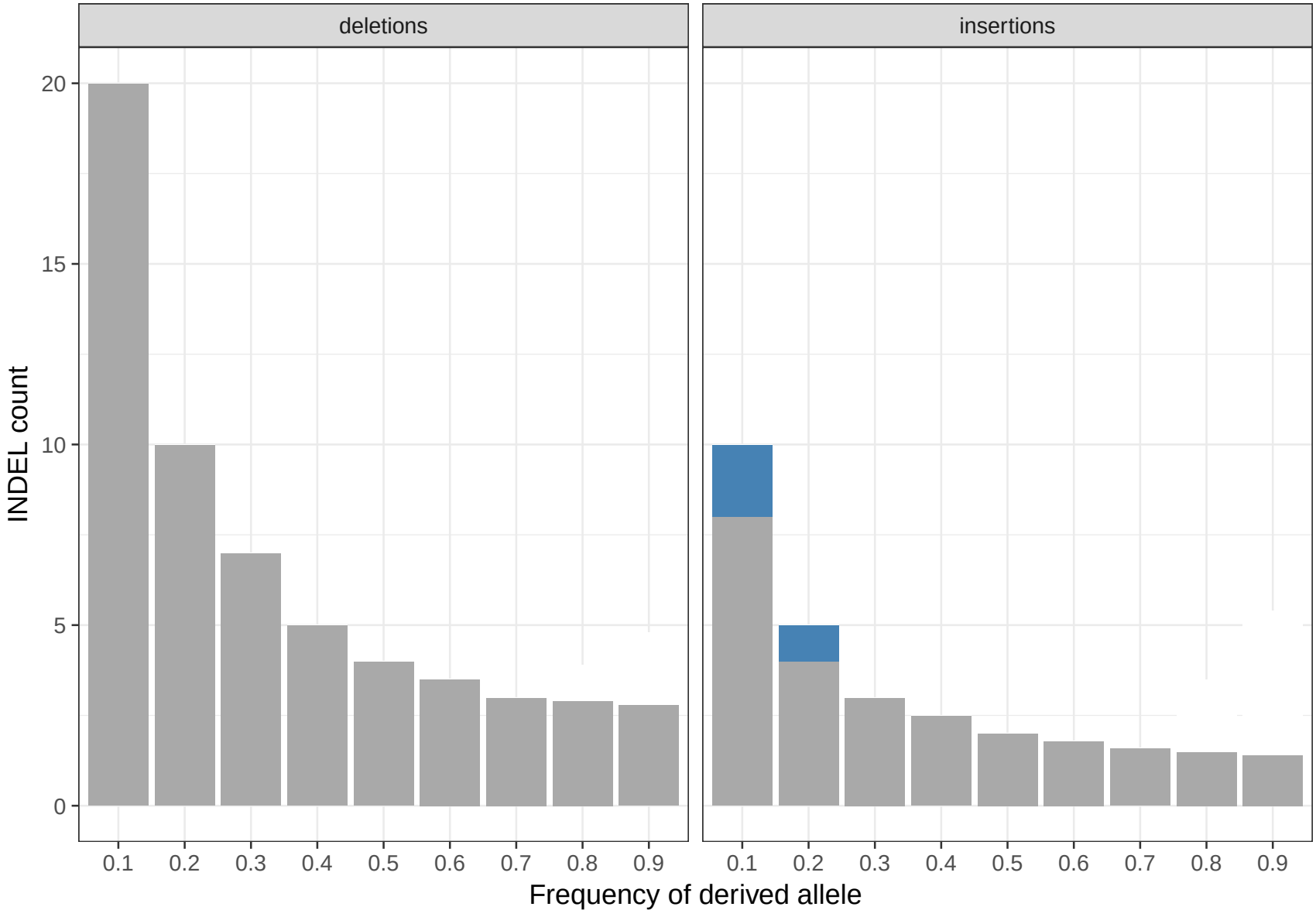

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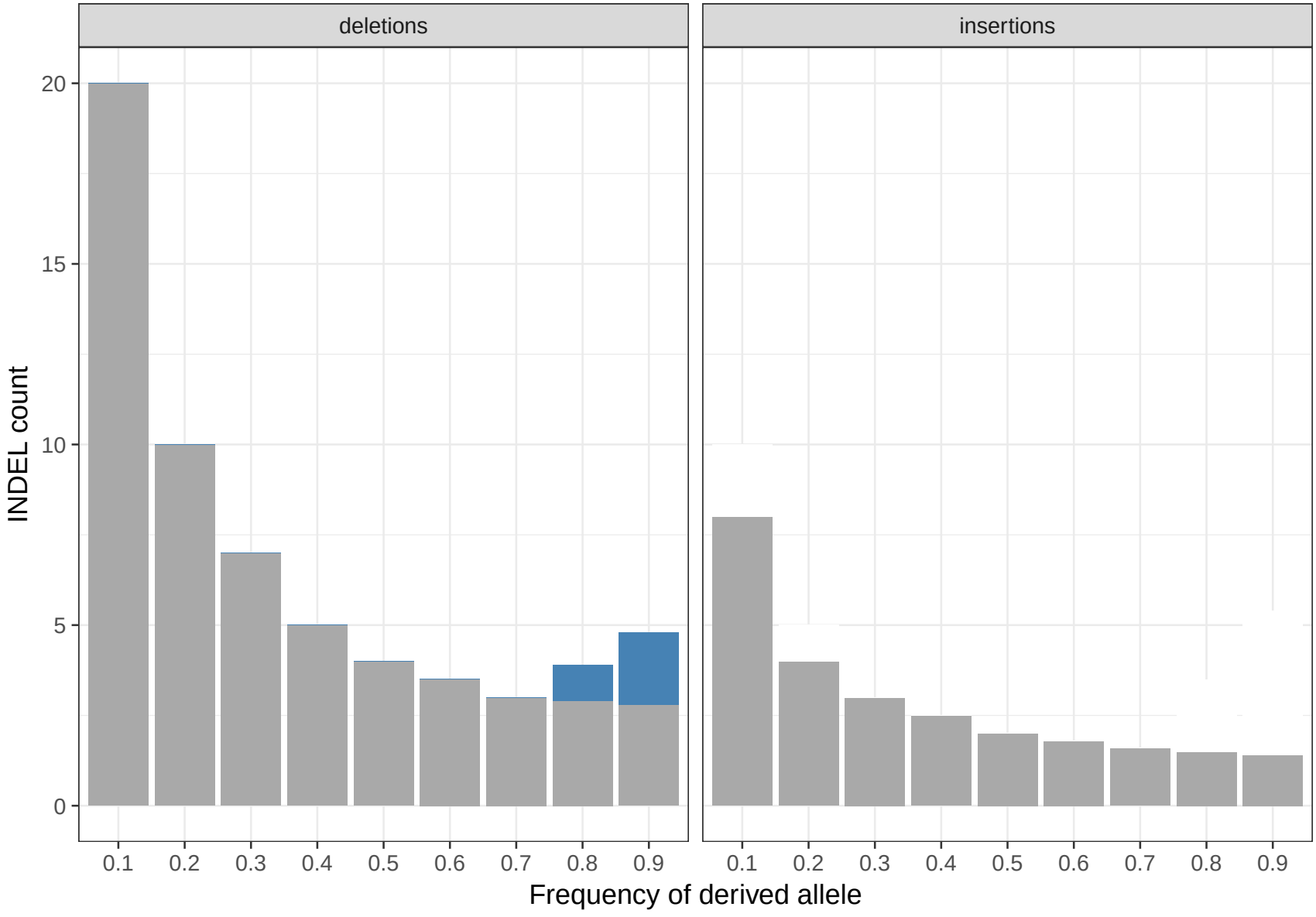

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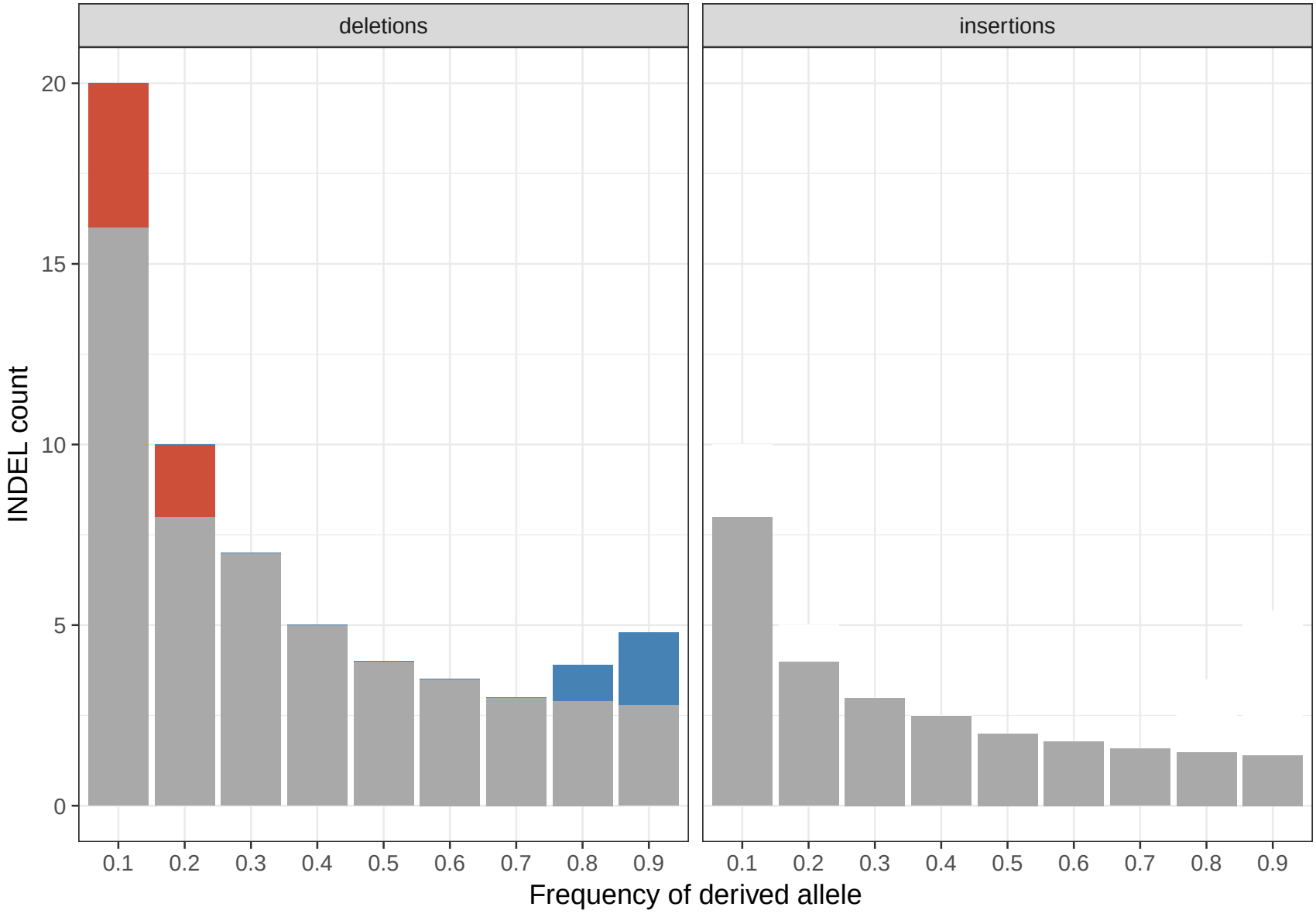

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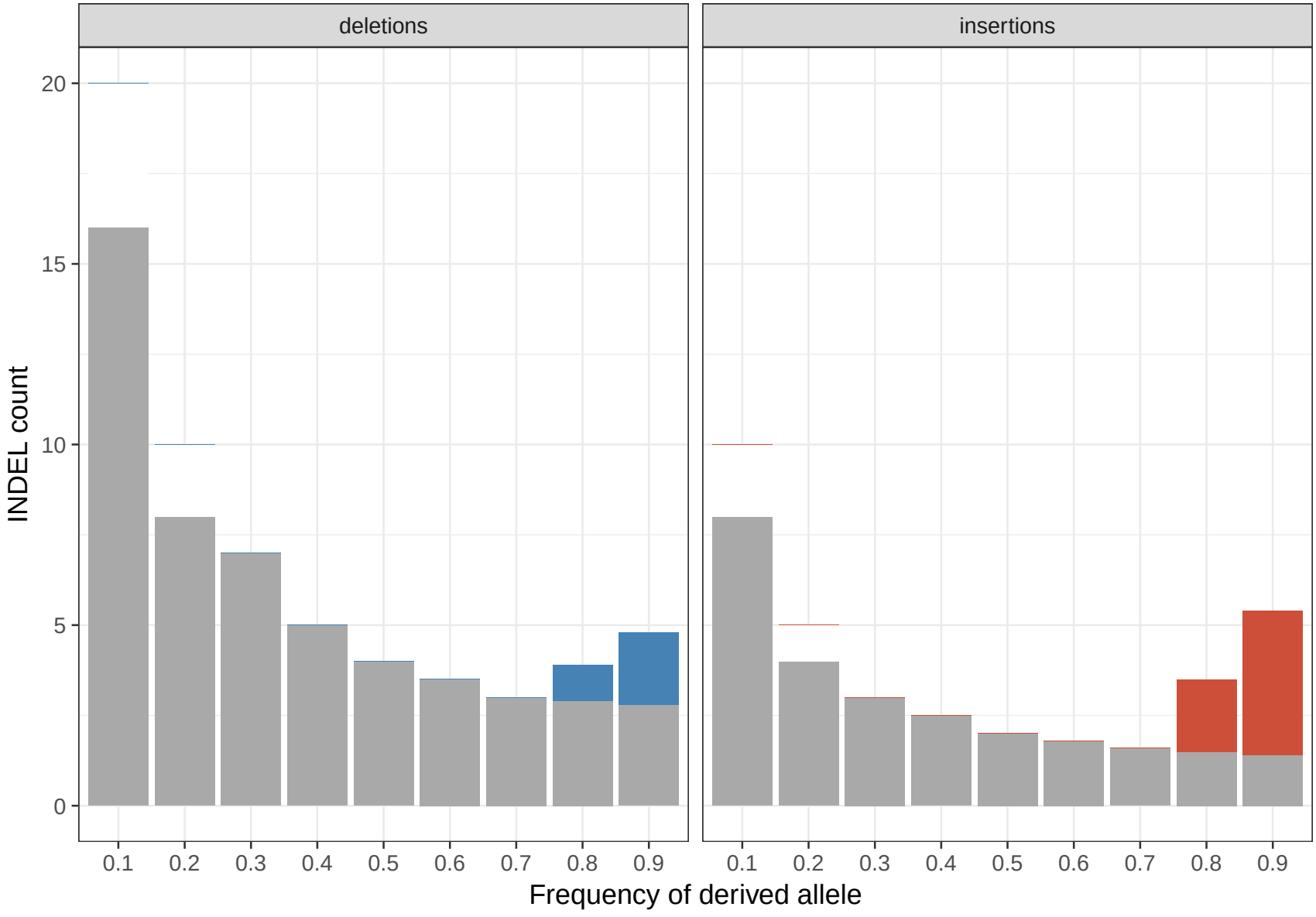

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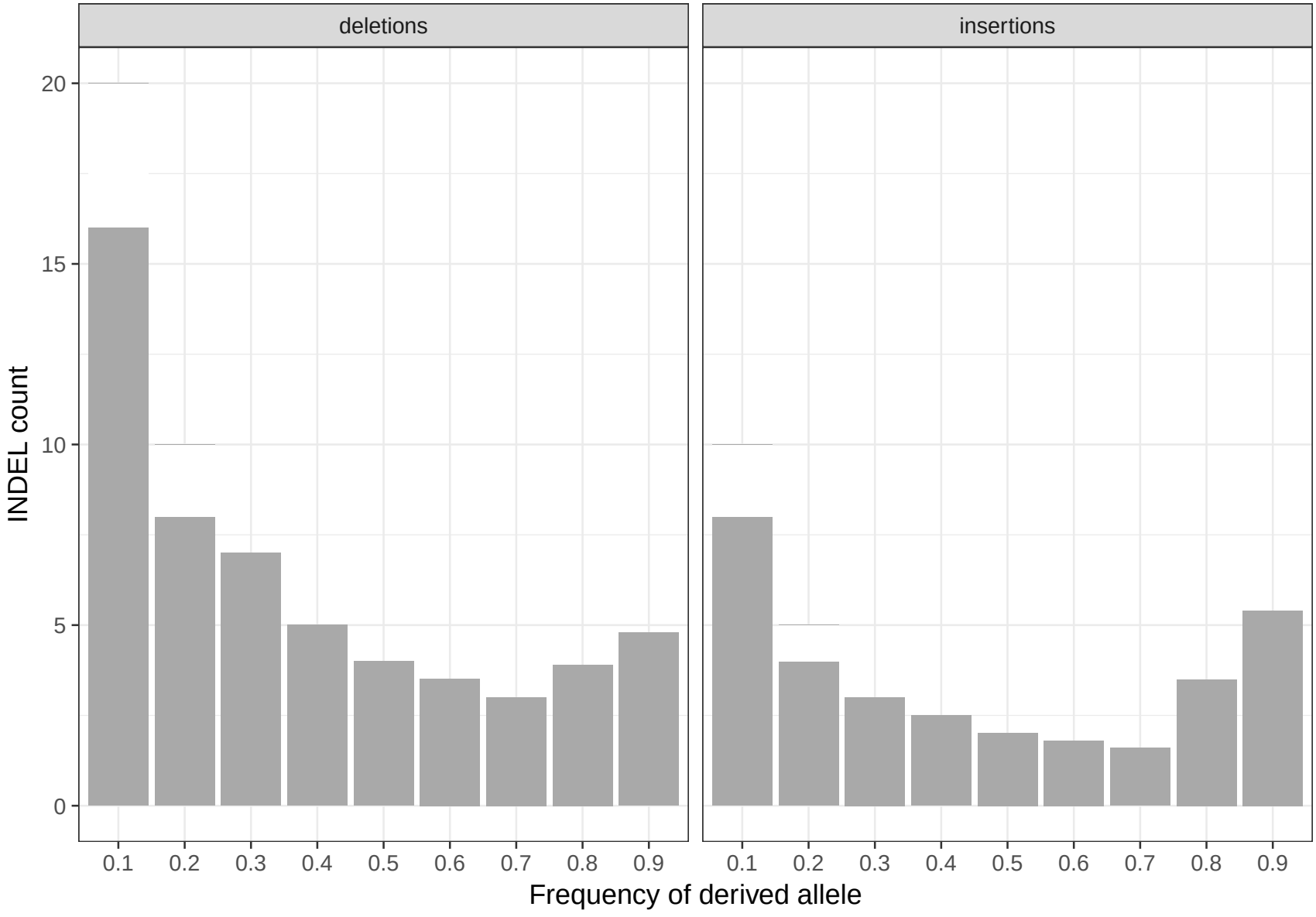


(see Hernandez et al., 2007)

Aims - make more specific

1. Quanitfy the selective and mutational pressures acting on INDELs in great tits (*Parus major*)
2. Investigate how these pressures vary in different genomic contexts, ie coding, non-coding, recombination rate.

Figure 2: tit

Advantages of an avian system

- Conserved karyotype and synteny - good for alignments
- Genomes consist of few large macrochromosomes and many small microchromosomes
- Results in a highly dynamic recombination landscape - power to associations with recombination

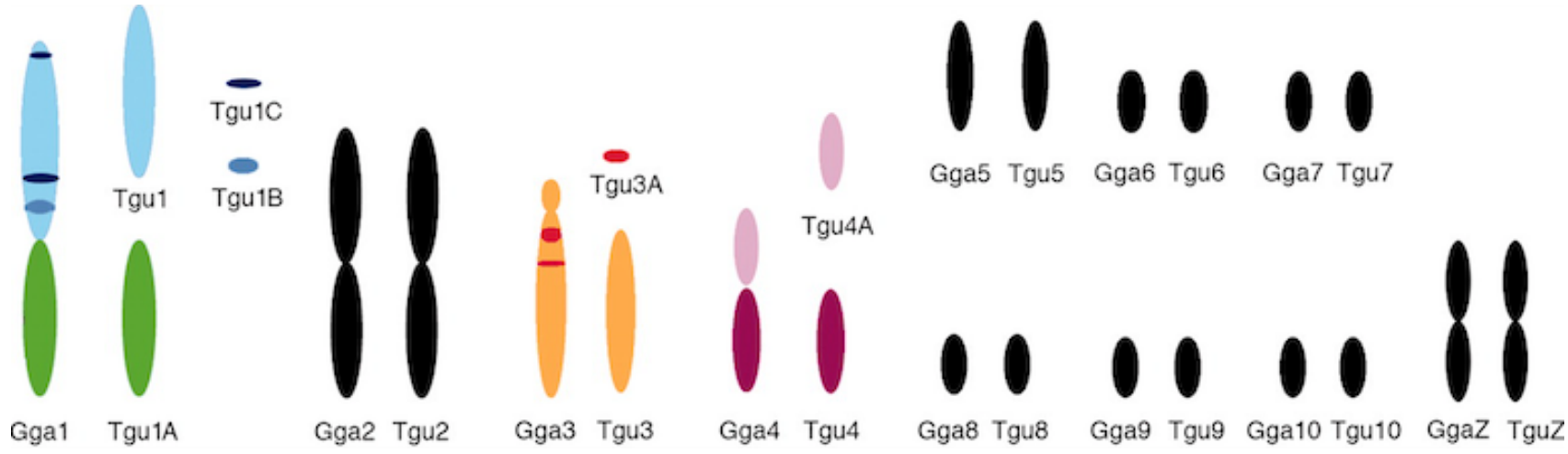


Figure 3: chroms

Data

Sample and pipeline

- 10 european great tit males (Corcoran et al., 2017)
- high coverage (44x)
- variant calling with GATK
- multispecies alignment between zebra finch, flycatcher and great tit
- parsimony based polarisation

The model - ‘anavar’

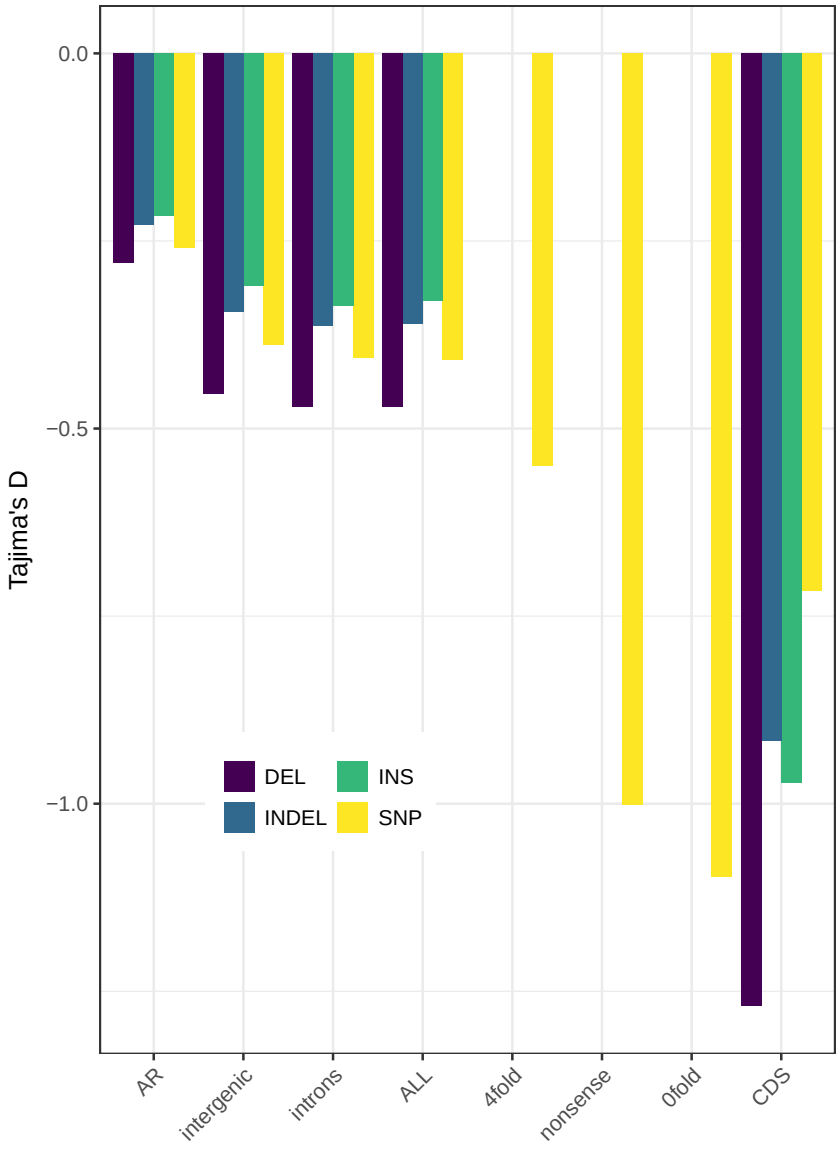
A novel maximum likelihood approach

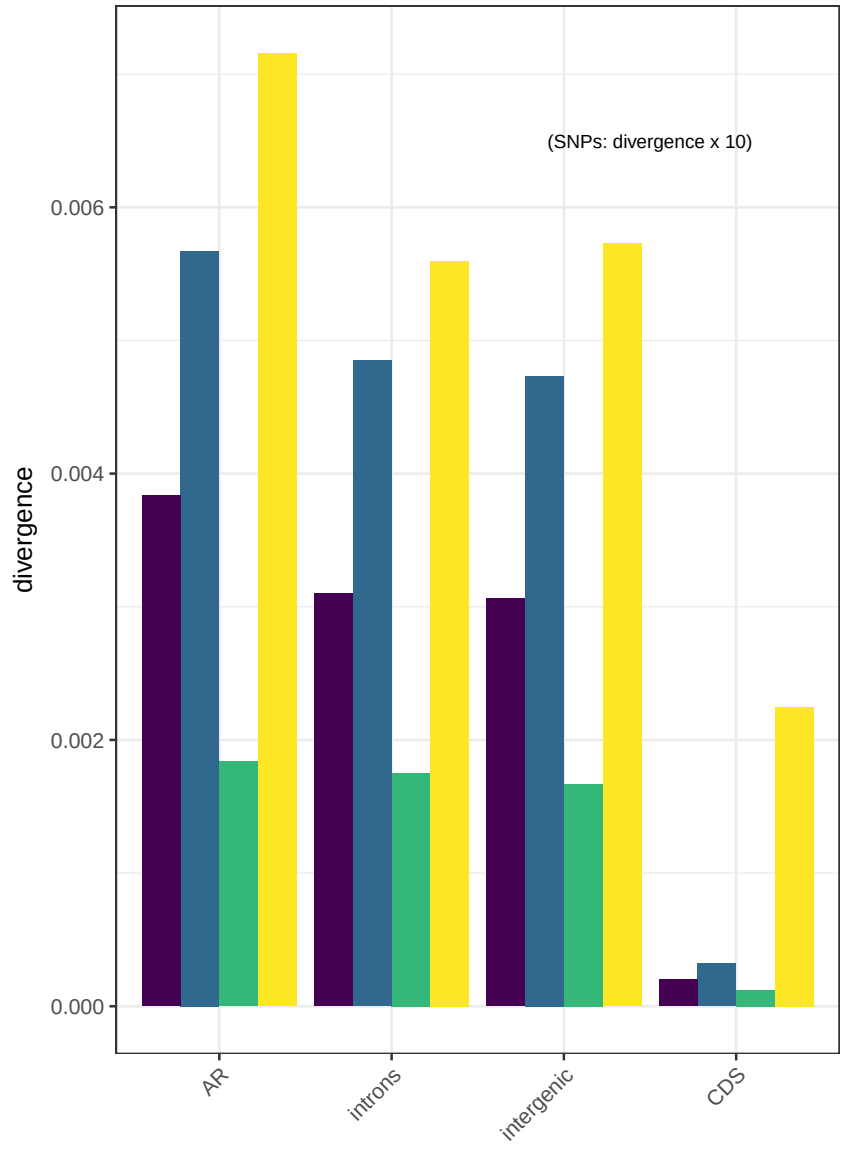
- takes the unfolded site frequency spectrum
- estimates for both insertions and deletions:
  - mutation rate ($\theta = 4N_e\mu$)
  - selection:
    - either selection coefficient ($\gamma = 4N_e s$)
    - or scale and shape paramater for distribution of fitness effects
  - polarisation error
- Controls for demography using neutral sites (Eyre-Walker et al., 2006)

(Barton and Zeng, 2018)

Dataset summary

Regional variation in purifying selection





Coding INDELs

Most INDELs extremely deleterious in coding regions

Moving away from genes

Approach

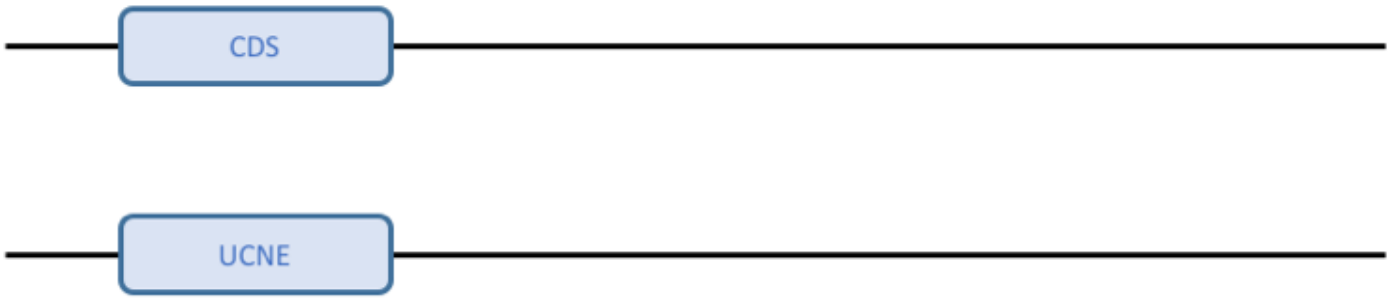


Figure 4: ls1

Approach

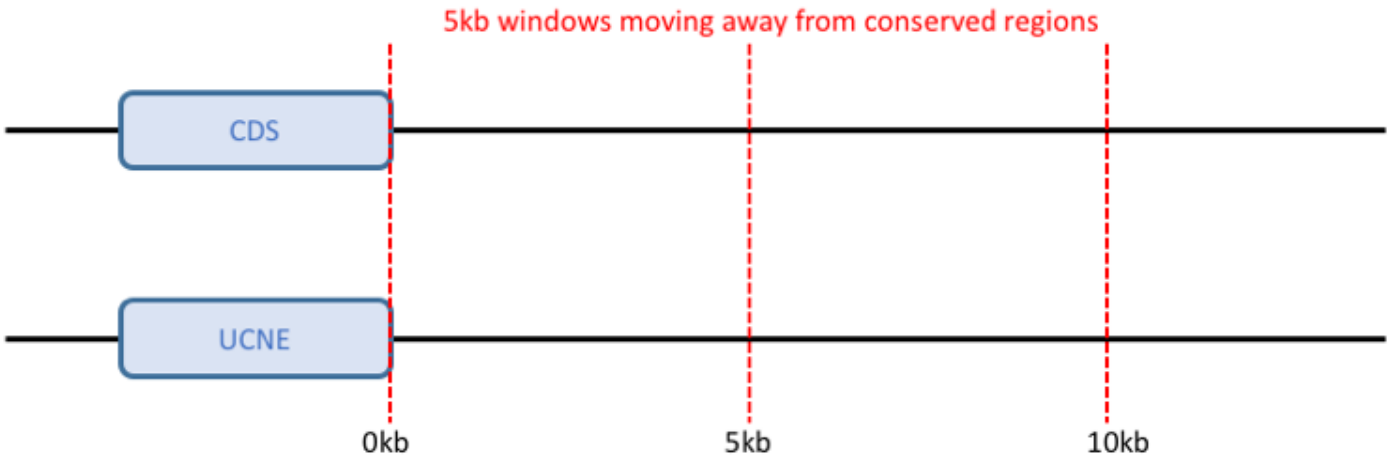


Figure 5: Is2

Approach

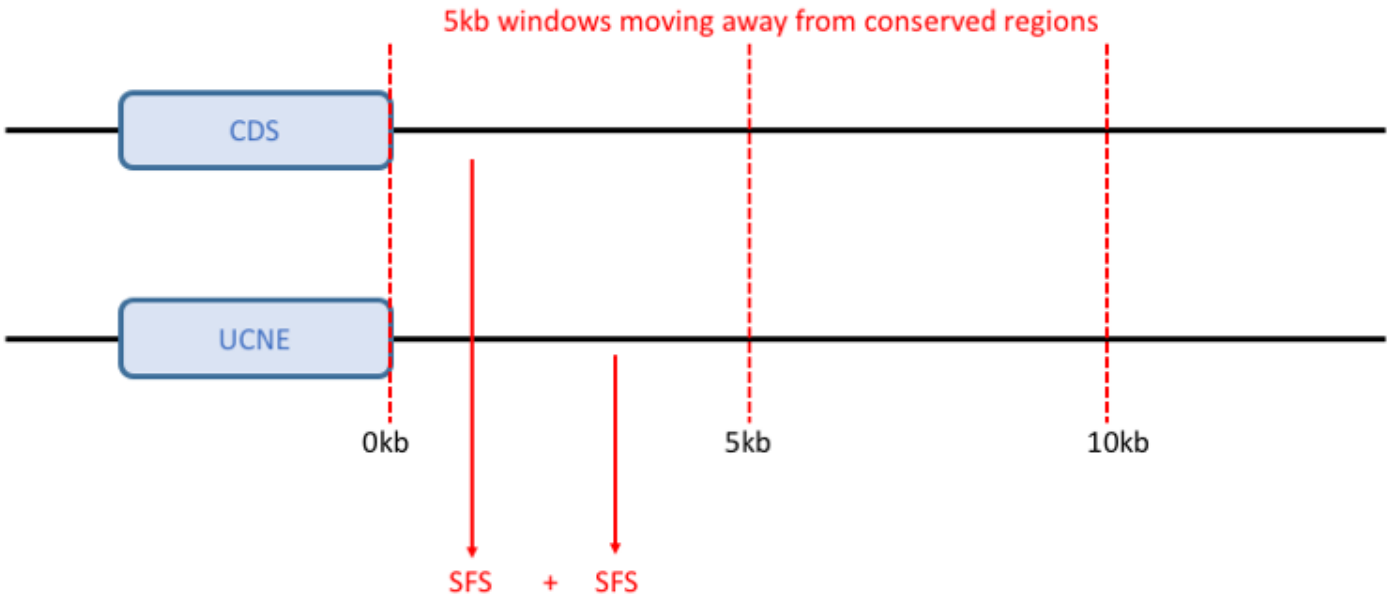


Figure 6: Is3

Approach

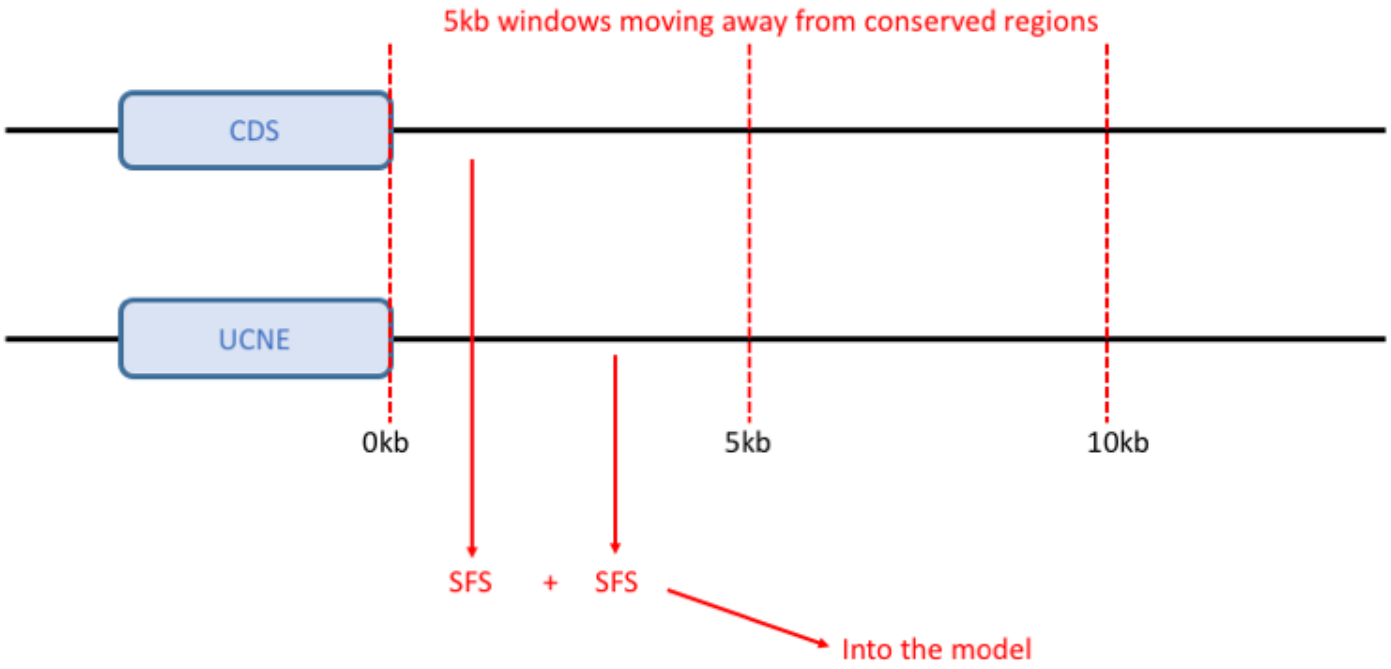


Figure 7: Is4

Evidence for linked selection

```
##
##  Spearman's rank correlation rho
##
## data:  as.numeric(ins_theta$ins_theta) and ins_theta$dis
## S = 14906, p-value = 0.04581
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.2842257

## [1] 50

##
##  Spearman's rank correlation rho
##
## data:  as.numeric(del_theta$del_theta) and del_theta$dis
## S = 10950, p-value = 0.0005822
## alternative hypothesis: true rho is not equal to 0
```

Recombination Analyses

Getting the data

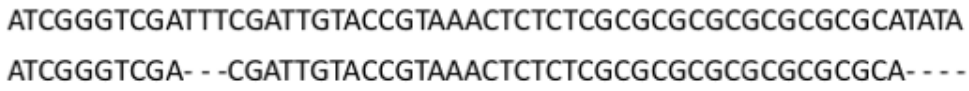


Figure 8: r1

Getting the data

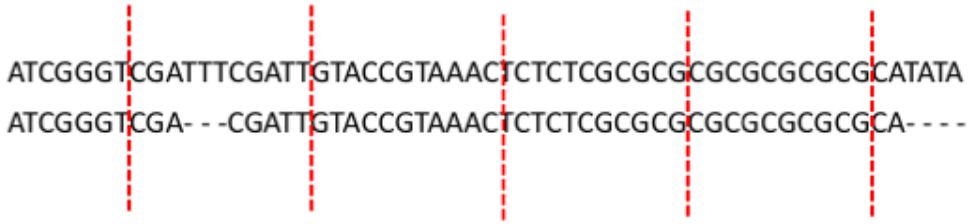


Figure 9: r2

Getting the data

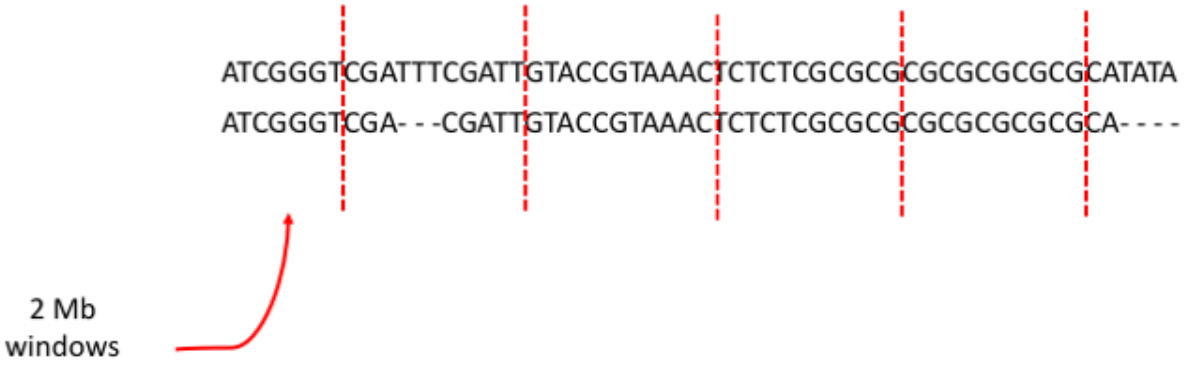


Figure 10: r3

Getting the data

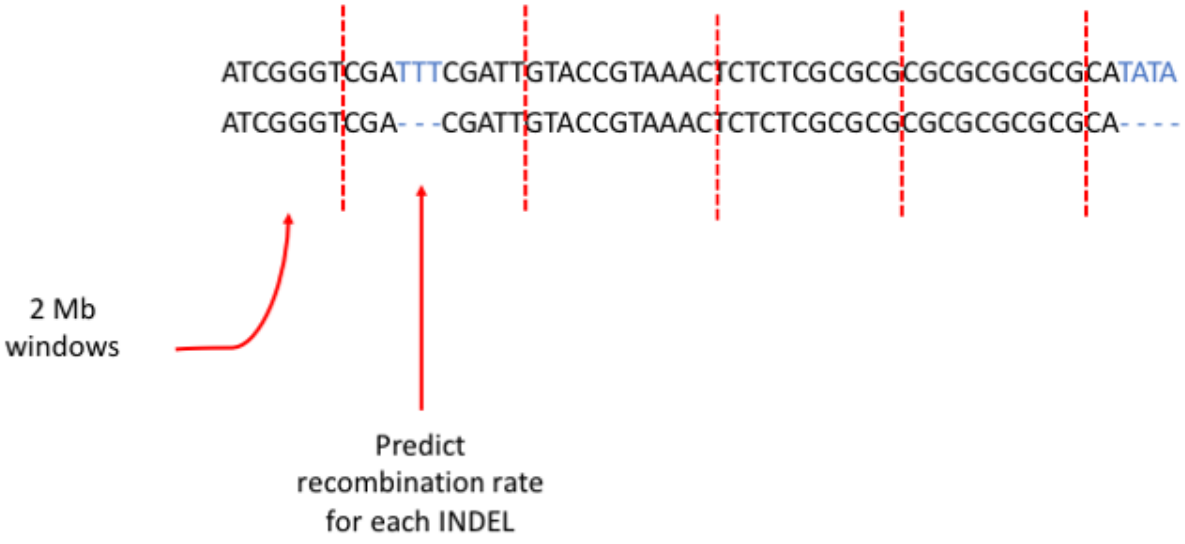
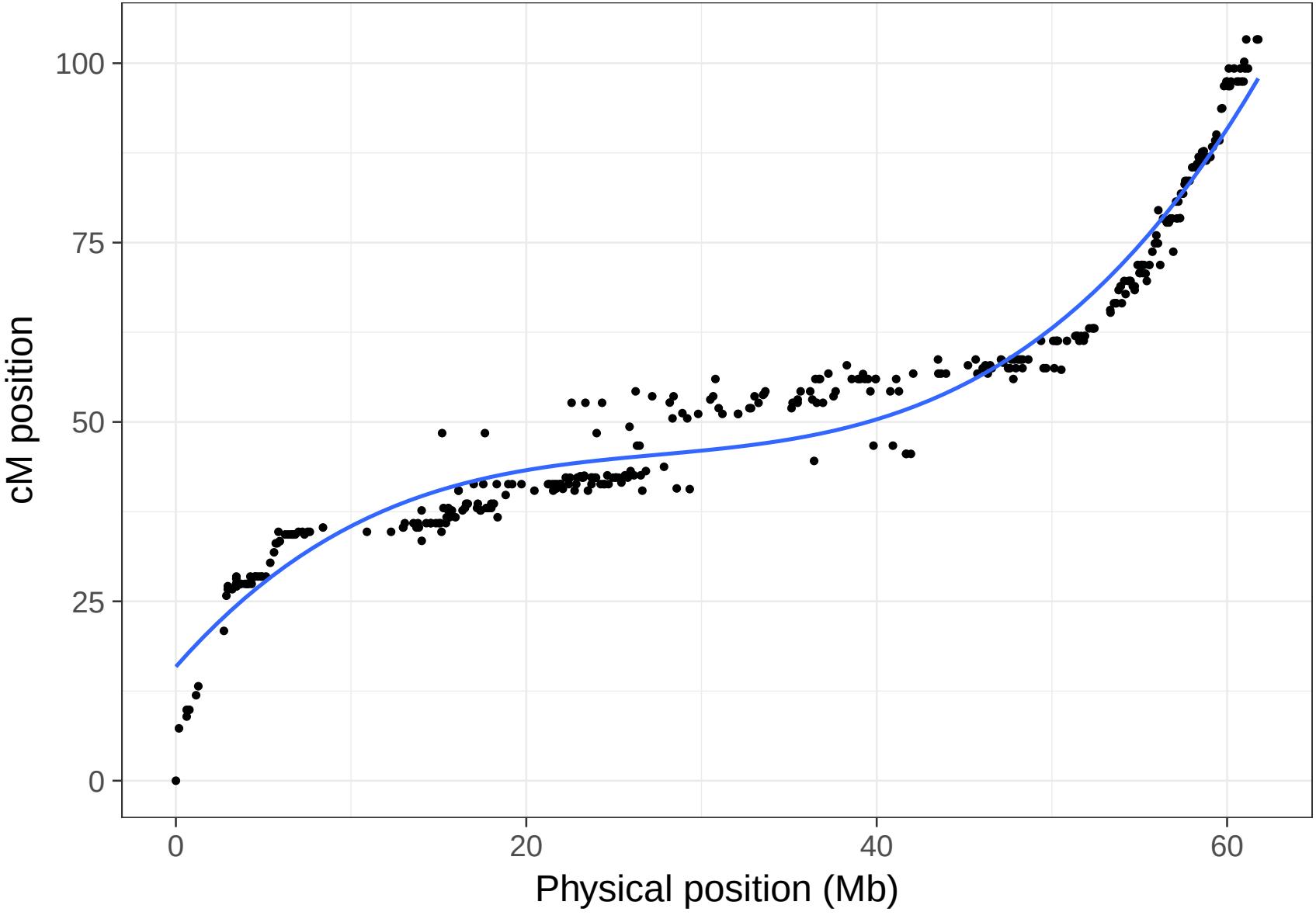


Figure 11: r4

Getting the data - recombination rate



Getting the data

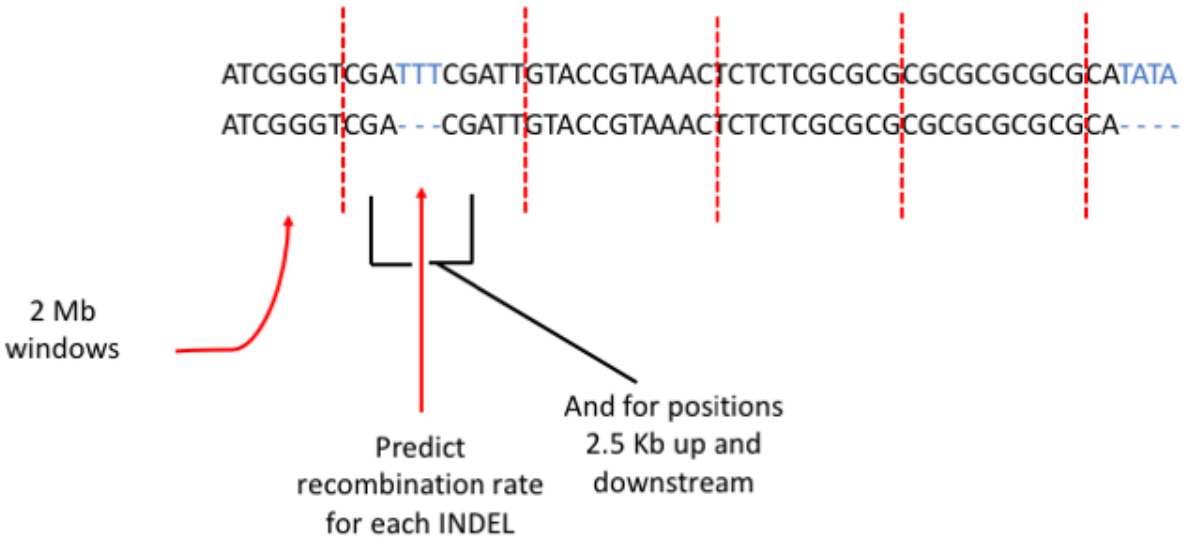


Figure 12: r5

Getting the data

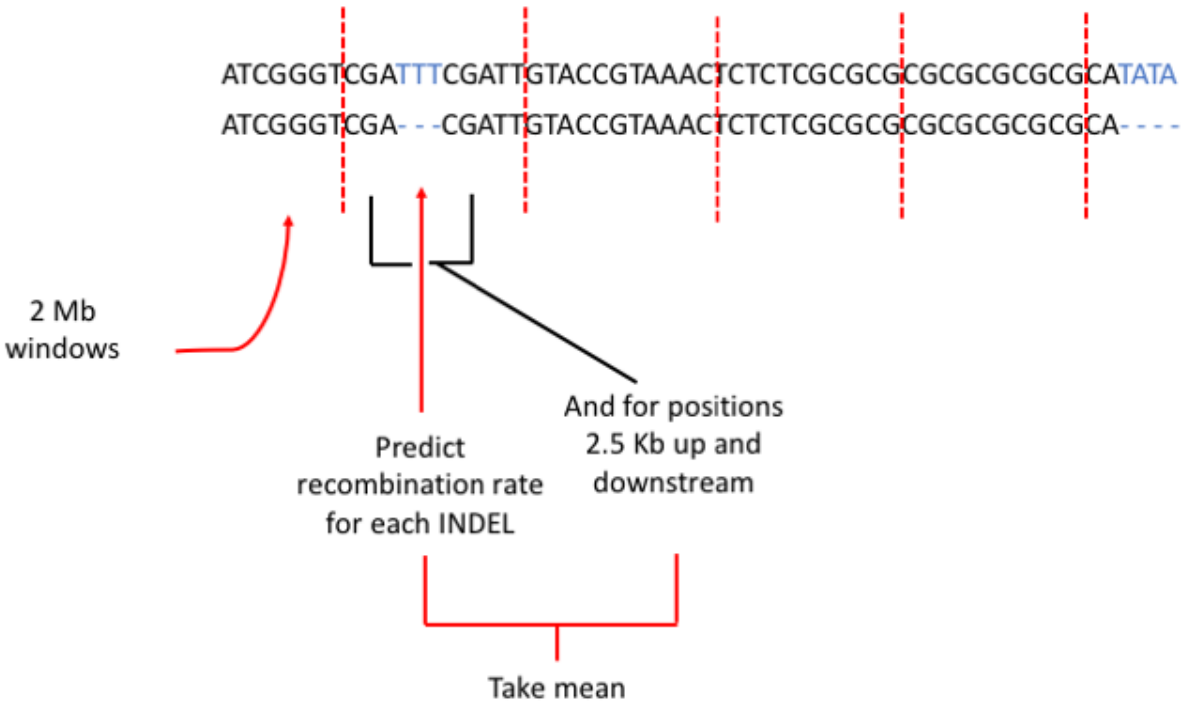


Figure 13: r6

Getting the data

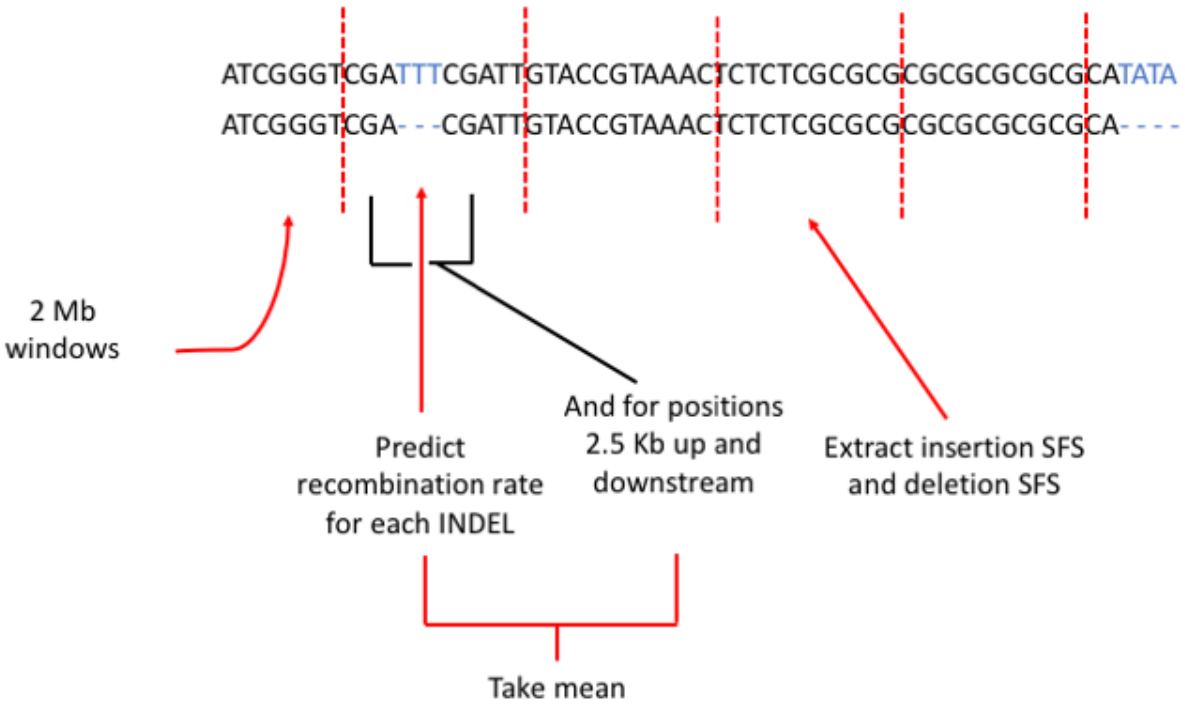


Figure 14: r7

Getting the data

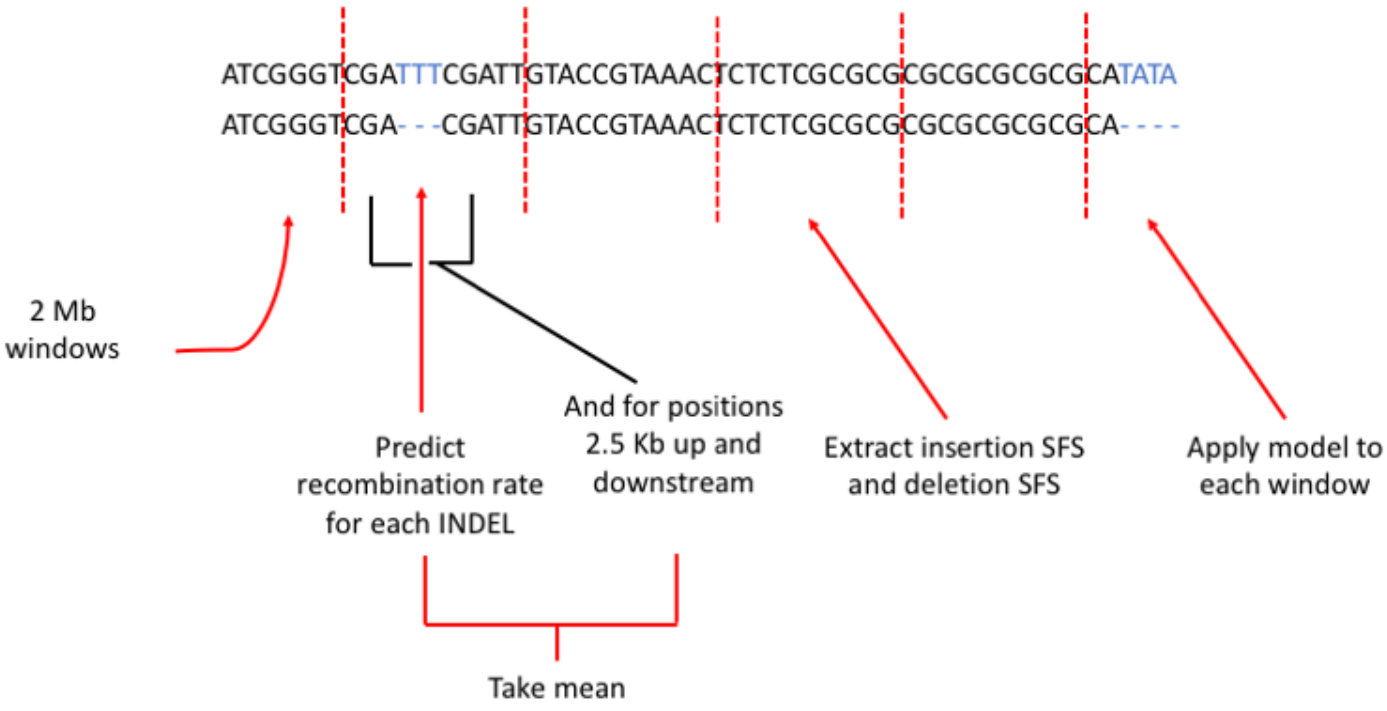


Figure 15: r8

Association between diversity and recombination

```
##
##  Spearman's rank correlation rho
##
## data:  window_data$tajd_ins and window_data$rec_rate
## S = 3969000, p-value = 3.725e-08
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
## 0.2998399

##
##  Spearman's rank correlation rho
##
## data:  window_data$tajd_del and window_data$rec_rate
## S = 3810100, p-value = 1.478e-09
## alternative hypothesis: true rho is not equal to 0
## sample estimates:
##       rho
```

Round up

Conclusion

- INDELs in genes are bad
- Don't find a link between recombination rate and deletion bias
- Linked selection appears to be constraining INDEL rates

Next steps

- Calculate alpha - proportion of substitutions fixed by positive selection
- Separate UCNE and CDS in linked selection analysis
- Any suggestions?

Questions?